Detection of Leptomeningeal CNS Metastases in Children

Noah D. Sabin, M.D.  Julie H. Harreld M.D.
Kathleen J. Helton M.D.  Zoltan Patay M.D., Ph.D.

St. Jude Children’s Research Hospital
Memphis, TN
Leptomeningeal Metastases:

Spread of tumor to the leptomeninges and associated tumor seeding of the cerebrospinal fluid (CSF)
Leptomeningeal Metastases: Mechanisms

- Direct contact with or extension into CSF
  - Tumor location (e.g. intraventricular)
  - Tumor erosion through pia, dura or ependyma
  - Tumor spread along perivascular (Virchow-Robin) spaces
  - Perineural spread of tumor
  - Seeding of CSF from surgery/procedure

- Hematogenous dissemination may allow tumor cells to reach the brain, choroid plexus and meningeal vessels with subsequent spread of tumor to subarachnoid space
Importance of Leptomeningeal Metastasis Detection

• Prognosis

• Guidance of Therapy

• MRI detection of leptomeningeal metastases may have greater correlation with survival than CSF cytology.* (CSF cytology, however, is still routinely performed.)

MRI Appearance of Leptomeningeal Metastases

• Diffuse linear enhancement

• Enhancing nodules along sulci, cranial nerves and ventricles
Differential Diagnosis:

- Leptomeningeal metastases
- Meningitis (including tuberculous meningitis)
- Viral encephalitis
- Neurosarcoid
- Post-trauma, post-surgery
Challenges in Leptomeningeal Metastasis Detection in Children

- Metastases are often tiny
- They may not enhance
- Small size of pediatric patients
- Need to efficiency – obtain enough sequences for metastasis detection without being overwhelmed with noncontributory imaging
- Want to increase sensitivity and increase spatial resolution
Techniques for Detecting Leptomeningeal Metastases in the CNS

• Subtraction imaging of the brain
• Post gadolinium FLAIR imaging of the brain
• Diffusion weighted imaging of the brain
• Thin section imaging and interleaving of sagittal spine images
• 3D imaging with multiplanar reformations
Subtraction Images

• Subtract precontrast T1-weighted images from postcontrast T1-weighted images to better visualize subtle enhancement.

• Helpful for detection of leptomeningeal metastases, infiltrating tumor and for differentiating enhancement from mineralization.
Use of Subtraction Images

Subtraction images best demonstrate enhancement of infiltrating tumor (arrows) in this 12 year old with gliomatosis cerebri.
Subtracting pre-contrast T1WI from the T1WI increases conspicuity of enhancing leptomeningeal metastasis (arrows) and perineural spread (along CN7, circled).

Use of Subtraction Images for Leptomeningeal Metastases
Post Gadolinium FLAIR Imaging of the Brain

- Improves detection of leptomeningeal metastases
  - Suppression of CSF signal
  - Decreased or absent vascular enhancement of sulcal vessels
  - T1 shortening from gadolinium increases conspicuity of disease
  - T2 hyperintensity of some metastases may improve detection
  - Effects underlying technique are likely additive
19 year old with anaplastic astrocytoma – FLAIR has T1 and T2 contributions; at standard dose, T1 effect of gadolinium predominates on post-contrast FLAIR (right). T2 hyperintensity of some metastases is also exploited, increasing chance of visualization. The effects may also be additive.
12 year old with leptomeningeal PNET – Post Gadolinium FLAIR images demonstrate scattered leptomeningeal metastases in the sulci (arrows).
Diffusion-Weighted Imaging

- Assists in detecting hypercellular metastatic lesions, particularly nonenhancing lesions

- Highlights tissue with water diffusion less than that of adjacent brain which, in the proper clinical context, is consistent with metastatic hypercellular tumor such as medulloblastoma
16 year old with metastatic medulloblastoma – the FLAIR images demonstrate subtle hyperintensity and thickening (arrows) of the bilateral parasagittal frontal cortices without significant enhancement on the post gadolinium T1-weighted images.
16 year old with metastatic medulloblastoma – diffusion-weighted images demonstrate restricted water diffusion in the bilateral parasagittal frontal cortices which, in this clinical context, is compatible with metastatic disease.
“Fill in the Gap” Technique for Spine MRI

• Better for detection of leptomeningeal metastases than standard MRI examination.
• Helps discriminate between metastases and blood vessels
• Imaging time at our institution for detection of metastases is less than with most standard techniques
“Fill in the Gap” Technique

• Allows acquisition of 3 mm slices at 1.5 mm intervals

• Perform usual sagittal postcontrast T1-weighted sequence using 3 mm sections with zero gap

• Repeat the same sequence dropping one slice (repeat sequence has one slice less than the original)

• The two sequences are interleaved to give 1.5 mm effective slice thickness with 1.5mm overlap
Improved Detection of Leptomeningeal Metastases with “Fill in the Gap” Technique

3 year-old with metastatic low grade astrocytoma. MRI spine without “fill in the gap” technique shows a few possible leptomeningeal metastases (arrows). Total imaging time for entire spine MRI: ~1 hour 35 minutes
Improved Detection of Leptomeningeal Metastases with “Fill in the Gap” Technique

T1 +C interleaved 1.5mm (effective), 1.5mm overlap

3 year-old with metastatic low grade astrocytoma. MRI spine with “fill in the gap” technique allows for more confident detection of more leptomeningeal metastases (arrows). Total imaging time for entire spine MRI: 35 minutes
Improved Detection of Leptomeningeal Metastases with “Fill in the Gap” Technique

MRI spine without “fill in the gap” technique shows nonspecific mild nodularity along the distal spinal cord (arrows).

T1 +C w/fat sat 3mm, 1mm gap

3 year-old with metastatic low grade astrocytoma. MRI spine without “fill in the gap” technique shows nonspecific mild nodularity along the distal spinal cord (arrows). Total imaging time for entire spine MRI: ~1 hour 35 minutes
Improved Detection of Leptomeningeal Metastases with “Fill in the Gap” Technique

3 year-old with metastatic low grade astrocytoma. MRI spine with “fill in the gap” technique allows for more confident detection of multiple leptomeningeal metastases (arrows). Total imaging time for entire spine MRI: 35 minutes.

T1 +C interleaved 1.5mm (effective), 1.5mm overlap
Usefulness of “Fill in the Gap” Technique for Normal Studies

MRI spine without “fill in the gap” technique: T1 +C 3mm, no gap

3 year-old with pineoblastoma - Metastases?
3 mm thick sections at 3 mm intervals demonstrate nodularity (arrows) along the lower spinal cord, easily mistaken for metastasis.
Usefulness of “Fill in the Gap” Technique for Normal Studies

MRI spine with “fill in the gap” technique:
T1 +C interleaved 1.5mm (effective), 1.5mm overlap

3 year-old with pineoblastoma - Metastases?
The enhancement appears smoother and is more confidently attributed to vascular structures. The patient underwent a pineal lesion biopsy but no other treatment between the 2 studies.
VIBE Images

- Volumetric Interpolated Breath Hold Examination (Siemens)/Fast Acquisition with Multiphase EFGRE3D (FAME – GE)/ T1W High Resolution Isotropic Volume Examination (THRIVE – PHILIPS)
- A volumetric T1-weighted pulse sequence often used for body imaging applications has also been used for visualization of neural foraminal structures. We use it for detection of leptomeningeal metastatic disease and for differentiation between blood vessels and metastases.
- Allows better visualization of contents of thecal sac with markedly decreased CSF flow-related artifact.
- Less time for same coverage
  - 160 3mm axial images, no gap:
    - T1 TSE with iPat: ~25 minutes
    - VIBE: ~11 minutes
Use of VIBE Sequences

19 year old with metastatic pleomorphic xanthoastrocytoma - a leptomeningeal metastasis along the spinal cord is suboptimally visualized due to CSF flow-related on the post-gadolinium fat saturated axial T1 TSE image (arrow, center). The CSF flow artifact is also demonstrated on the precontrast axial T1 TSE image (left). The postcontrast axial T1-weighted VIBE pulse sequence (right) reveals the enhancing metastasis without significant flow-related CSF artifact.
Value of CISS/FIESTA-C

- CISS (Siemens)/FIESTA-C (GE) [Constructive Interference in the Steady State/Fast Imaging Employing Steady State Acquisition-C]
- These 3D sequences provide excellent spatial resolution between cerebrospinal fluid and adjacent structures
- Helpful for distinction between leptomeningeal metastases along the spinal cord and nearby structures such as blood vessels and protruding intervertebral disks
Sagittal and axial postcontrast T1 weighted images of the spine of a 15 year old with a history of anaplastic ependymoma demonstrate an enhancing nodular structure (arrows) along the anterior aspect of the spinal cord at the T5-T6 level. Diagnostic considerations include a leptomeningeal metastasis, disk protrusion or prominently enhancing epidural venous plexus.
Value of CISS

Sequential axial CISS images through the T5-T6 level of the same patient allow determination that the structure along the cord represents an enhancing intervertebral disk protrusion.
Pitfalls

Anesthesia and supplemental oxygen effects can be confused for disease on FLAIR imaging.

Hyperintensity in the sulci on pre- and post-gadolinium FLAIR images may be seen in patients receiving sedation and can mimic leptomeningeal metastatic disease.
Pitfalls

Motion can cause false hyperintensity that may be confused with enhancement on subtraction images.

If the patient changes position, even slightly, between pre- and post-gadolinium T1-weighted images, hyperintensities may be present on subtraction images that can be confused for enhancement (arrows).
Pitfalls

Blood products can be confused for restricted diffusion on diffusion-weighted images
The brighter signal on DWI (and darker appearance on ADC map) of residual blood products may help to distinguish them from residual tumor.

7 year old with medulloblastoma.
Routine Brain imaging at St. Jude

BW=Band Width in Hz/Pixel (Siemens). To convert to kHz (GE):

\[
\text{Hz/pixel BW} \times \text{Base Resolution (RO Matrix)} = A \\
A/2 \times 0.001 = \text{Bandwidth in kHz}
\]
Routine Spine, Leptomeningeal Screen

*Non-contrast sagittal T1WI acquired only at initial visit or for trouble-shooting.

Post spine SAG T1 interleaved (x2) technique:
• Repeat POST-SAG-T1 twice at the same prescription location, *dropping one slice* (can acquire “in between” locations).
• ~20 and 21 slices at the same location (may differ with patient size)

**Eliminating the gap is critical.**
A 1mm metastasis can change risk stratification and management and could be entirely missed with a gap.